

This listing of claims will replace all prior versions, and listings, of claims in the application.

**Listing of Claims:**

1. (Currently Amended) A composition comprising a recombinant polynucleotide that encodes a modified Factor VII, said modified Factor VII comprising wherein the modification comprises a proteolytic cleavage site at a location that allows secretion of active Factor VII upon cleavage, said proteolytic cleavage site having the sequence Arg-Lys Arg Arg-Lys Arg Arg-Lys-Arg-Arg-Lys-Arg (as set forth in SEQ ID NO: 1) and not normally present in Factor VII, and wherein Factor VII is cleaved at the proteolytic cleavage site is introduced at a location that allows secretion of active Factor VII when expressed in an animal cell and secreted in an active form.
2. (Previously Presented) The composition of claim 1, wherein the Factor VII is a functional variant or a functional subsequence of a naturally occurring Factor VII.
- 3.-12. (Cancelled)
13. (Previously Presented) The composition of claim 1, wherein the proteolytic cleavage site is introduced between amino acids 152 and 153 of Factor VII.
14. (Previously Presented) The composition of claim 1, wherein the proteolytic cleavage site is introduced between arginine 152 and isoleucine 153 of Factor VII.
15. (Original) The composition of claim 1, wherein the animal cell is mammalian.
16. (Original) The composition of claim 15, wherein the mammalian cell is human.
17. (Previously Presented) The composition of claim 2, wherein the functional variant has one or more conservative amino acid substitutions of wild type Factor VII.
18. (Original) The composition of claim 2, wherein the functional variant comprises a Factor VII having increased activity relative to wild type Factor VII.
19. (Original) The composition of claim 2, wherein the functional variant comprises a

Factor VII having increased stability *in vivo* relative to wild type Factor VII.

20. (Original) The composition of claim 2, wherein the functional variant comprises a Factor VII having decreased immunogenicity relative to wild type Factor VII.

21. (Previously Presented) The composition of claim 1, wherein the Factor VII is mammalian.

22. (Previously Presented) The composition of claim 21, wherein the Factor VII is primate, canine, feline, porcine, equine or bovine.

23. (Original) The composition of claim 22, wherein the primate is human.

24. (Previously Presented) The composition of claim 1, wherein the recombinant polynucleotide encoding the modified Factor VII is operatively linked to a regulatable or tissue specific expression control element.

25. (Original) The composition of claim 24, wherein the regulatable or tissue specific expression control element comprises a promoter.

26. (Original) The composition of claim 24, wherein the promoter comprises a skeletal muscle actin promoter or a muscle creatine kinase promoter.

27. (Original) The composition of claim 24, wherein the tissue specific expression control element confers expression of the modified blood clotting factor in muscle, liver, kidney or blood vessel endothelium.

28. (Original) The composition of claim 24, wherein the regulatable expression control element comprises elongation factor 1 $\alpha$  promoter.

29. (Currently Amended) A The composition comprising a vector and the recombinant polynucleotide of claim 1, ~~further comprising a vector~~.

30. (Original) The composition of claim 29, wherein the vector comprises a vector

suitable for introduction into a cell *in vivo*.

31. (Original) The composition of claim 30, wherein the vector comprises an adeno associated virus (AAV), adenovirus, retrovirus, parvovirus, papilloma virus, reovirus, rotavirus or a herpes virus.

32. (Original) The composition of claim 30, wherein the vector comprises a plasmid vector.

33. (Withdrawn) A polypeptide encoded by the recombinant polynucleotide of claim 1.

34. (Currently amended) A kit comprising a composition of claim 1 or ~~a polypeptide of claim 33~~.

35. (Original) A kit comprising a composition of claim 1 further including instructions for expressing the modified blood clotting factor *in vitro*, *ex vivo* or *in vivo*.

36. (Withdrawn) The composition of claims 1 or 33, further comprising a cell.

37. (Withdrawn) The composition of claim 36, wherein the cell is a muscle, liver, kidney or blood vessel cell.

38.-40. (Cancelled)

41. (Previously Presented) The composition of claim 1, further comprising a pharmaceutically acceptable carrier.

42. (Withdrawn) A method for treating a bleeding or clotting disorder of a subject having or at risk of having a bleeding or clotting disorder comprising administering to the subject an amount of the composition of claim 1 sufficient to ameliorate one or more symptoms of the disorder.

43. (Withdrawn) The method of claim 42, wherein the disorder is amenable to treatment with Factor VII, Factor VIII or Factor IX.

44. (Withdrawn) The method of claim 42, wherein the disorder is caused by insufficient activity or expression of a vitamin-K dependent procoagulant.
45. (Withdrawn) The method of claim 42, wherein the disorder is caused by insufficient platelet aggregation.
46. (Withdrawn) The method of claim 42, wherein the disorder comprises hemophilia or Factor VII deficiency.
47. (Withdrawn) The method of claim 46, wherein the hemophilia comprises hemophilia A or hemophilia B.
48. (Withdrawn) The method of claim 42, wherein the disorder comprises Glanzmann's thrombasthenia.
49. (Withdrawn) The method of claim 42, wherein the disorder comprises Bernard Soulier's thrombasthenia.
- 50.-55. (Cancelled)
56. (Withdrawn) A method of decreasing clotting time in a subject in need of decreased clotting time comprising administering to the subject an amount of the composition of claim 1 sufficient to decrease clotting time in the subject,
57. (Withdrawn) The method of claim 56, wherein the modified blood clotting factor comprises Factor VII, Factor VIII or Factor IX.
58. (Withdrawn) The method of claim 56, wherein the subject is a mammal.
59. (Withdrawn) The method of claim 58, wherein the mammal is human.
60. (Withdrawn) A method of reducing the frequency or severity of bleeding in a subject in need of reduced frequency or severity of bleeding comprising

administering to the subject an amount of the composition of claim 1 sufficient to reduce the incidence or severity of a bleeding in the subject.

61. (Withdrawn) The method of claim 60, wherein the composition comprises Factor VII, Factor VIII or Factor IX,
62. (Withdrawn) The method of claim 60, wherein the subject is a mammal.
63. (Withdrawn) The method of claim 62, wherein the mammal is a human.
64. (Withdrawn) A composition comprising a recombinant polynucleotide that encodes a modified Factor IX, wherein the modification comprises a proteolytic cleavage site having the sequence Arg Lys Arg Arg-Lys-Arg (SEQ ID NO:1) not normally present in Factor IX, and wherein Factor IX is cleaved at the cleavage site when expressed in an animal cell and secreted in an active form.
65. (Withdrawn) The composition of claim 64, wherein the Factor IX is a functional variant or a functional subsequence of a naturally occurring Factor IX.
66. (Withdrawn) The composition of claim 64, wherein the animal cell is mammalian.
67. (Withdrawn) The composition of claim 66, wherein the mammalian cell is human.
68. (Withdrawn) The composition of claim 65, wherein the functional variant has one or more conservative amino acid substitutions of wild type Factor IX.
69. (Withdrawn) The composition of claim 64, wherein the Factor IX is mammalian.
70. (Withdrawn) The composition of claim 69, wherein the Factor IX is primate, canine, feline, porcine, equine or bovine.
71. (Withdrawn) The composition of claim 70, wherein the primate is human.
72. (Withdrawn) The composition of claim 64, wherein the recombinant polynucleotide encoding the modified Factor IX is operatively linked to a

regulatable or tissue specific expression control element.

73. (Withdrawn) The composition of claim 72, wherein the regulatable or tissue specific expression control element comprises a promoter.

74. (Withdrawn) The composition of claim 72, wherein the promoter comprises a skeletal muscle actin promoter or a muscle creatin kinase promoter.

75. (Withdrawn) The composition of claim 72, wherein the tissue specific expression control element confers expression of the modified blood clotting factor in muscle, liver, kidney or blood vessel endothelium.

76. (Withdrawn) The composition of claim 72, wherein the regulatable expression control element comprises elongation factor 1a promoter.

77. (Withdrawn) The composition of claim 64, further comprising a vector.

78. (Withdrawn) The composition of claim 77, wherein the vector comprises a vector suitable for introduction into a cell *in vivo*.

79. (Withdrawn) The composition of claim 78, wherein the vector comprises an adeno associated virus (AAV), adenovirus, retrovirus, parvovirus, papilloma virus, reovirus, rotavirus or a herpes virus.

80. (Withdrawn) The composition of claim 77, wherein the vector comprises a plasmid vector.

81. (Withdrawn) A polypeptide encoded by the recombinant polynucleotide of claim 64.

82. (Withdrawn) A kit comprising a composition of claim 64 or a polypeptide of claim 81.

83. (Withdrawn) A kit comprising a composition of claim 64 further including instructions for expressing the modified blood clotting factor *in vitro*, *ex vivo* or

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**PATENT**

*in vivo.*

84. (Withdrawn) The composition of claims 64, further comprising a pharmaceutically acceptable carrier.